AUG 16 2005

510(K) SUMMARY

Duet™ system

510(k) Number K 050840

Applicant's Name:

Bioview Ltd.
3 Pekeris St. Rehovot
P.O.B. 4051,
Nes Ziona 70400, Israel
Tel: 972-8-9366868
Fax: 972-8-9366869

Contact Person:

Dorit Winitz, Ph.D.
Biomedical Strategy Ltd.
11 Menachem Begin Street.
Ramat Gan 52521, Israel
Tel: +972-3- 6123281
Fax: +972-3-6123282
Mail: dorit@ebms.co.il

Date Prepared:

March, 2005

Trade Name:

Duet™ System

Classification Name:

Automated cell-location device **and:**
Automated Fluorescence in situ Hybridization (FISH) Enumeration Systems

Classification:

FDA has classified Automated cell-locating devices (product code JOY, Regulation No. 864.5260) and Automated Fluorescence *in situ* Hybridization

(FISH) Enumeration Systems (product code NTH, Regulation No. 866.4700) as class II devices and they are reviewed by the Pathology and Immunology Panels, respectively.

Predicate Devices:

- Duet™ System, cleared under K030192, and K040591 (Product code JOY)
- Vysis UroVysion™ Bladder Cancer Recurrence Kit, cleared under K011031 and K033982 (Product code NOT)
- Human manual visualization of urine specimens cells from subjects with transitional cell carcinoma of the bladder, probed by the UroVysion™ Kit by conventional microscope.
- Vysis® AutoVysion™ System, K041875 (product code NTH)

Performance Standards:

No performance standards have been established for such device under Section 514 of the Federal Food, Drug, and Cosmetic Act. However, the Duet™ system complies with the following voluntary standards:

- EN 61010-1
- EN 61326-1
- IEC 60601-1-4
- EN-1441: Medical devices – Risk Analysis.
- ISO 14971 Medical Devices-Risk Management

Indications:

The Duet™ System is an automated scanning microscope and image analysis system. It is intended for in-vitro diagnostic use as an aiding tool to the pathologist in the detection, classification and counting of cells of interest based on color, intensity, size, pattern, and shape. The Duet™ System is intended to detect:

1. Hematopoietic cells stained by Giemsa stain, Immunohistochemistry or ISH (with bright field and fluorescent) prepared from cell suspension.
2. Amniotic cells stained by FISH (using direct labeled DNA probes for chromosomes X, Y, 13, 18 and 21).
3. Cells in urine specimens, stained by FISH (using the Vysis UroVysion™ Bladder Cancer Recurrence Kit for chromosomes 3, 7, 17 and 9p21 locus), from subjects with transitional cell carcinoma of the bladder.

Device Description:

The Duet™ System is a fully integrated imaging and scanning platform that automates time-consuming and difficult laboratory tasks of slide screening by making a significant reduction in time and labor currently required.

The Duet™ scans in high resolution and in full color cell samples at high speed both in bright light illumination and in fluorescent illumination.
Duet™ suggests classification of the cells according to their morphological features, their staining (Giemsa, IHC) and fluorescent signals, and allows the user to quickly examine the results, correct them as needed and generate a report summarizing the sample's data. The unique feature of the Duet system allows the presents combined presentation of morphological and specific staining information of the same cell, for all the cells of the sample.

Substantial Equivalence:

Intended use
The intended use of the Duet™ System is expanded to include the indication of an aiding tool in the detection of aneuploidy for chromosomes 3, 7, 17 and loss of the 9p21 locus via FISH in Urine specimens from subjects with transitional cell carcinoma of the bladder, probed by the Vysis UroVysion™ Bladder Cancer Recurrence Kit

Detection, classification and counting of urine specimens from subjects with traditional cell carcinoma of the bladder, stained using the cleared Vysis UroVysion™ Bladder Cancer Recurrence Kit are routinely performed manually by cytogeneticist using conventional microscopes, according to the kit instructions.

The claim of an automated aiding tool for detection and enumeration of FISH signals is also claimed by the 510(k)-cleared Vysis AutoVysion™ System and the previously cleared Duet™ System.

The Duet™ System employs the same procedures as employed by human manual visualization using conventional microscopes. Additionally, the new intended use was supported by a comparative performance study demonstrating that the operation of the Duet™ System is safe and effective as an aiding tool in the detection of aneuploidy for chromosomes 3, 7, 17 and loss of the 9p21 locus via FISH in urine specimens from subjects with transitional cell carcinoma of the bladder, probed by the Vysis UroVysion™ Bladder Cancer Recurrence Kit, in comparison to manual microscopy.

Technological characteristics

The current Duet™ System is the same system as the 510(k)-cleared Duet™ System. No changes were incorporated to the system's hardware or software to support the new indication.

Mode of Operation

Exactely as the cleared Duet™ System, the current Duet™ System provides two modes of operation:

- Automatic scanning: provides a gallery of targets that the system captures for all identified cells.
- Manual scanning: provides interactive control over the microscope. This enables a user-controlled scan of any slide under either bright field or fluorescent illumination.

The user of the current Duet™ Systems, enters the scan parameters, slide number, comments, and annotates the results in the same manner as done using the predicate devices and during standard human visualization of cytology slides. Similarly, final classification is performed by the operator.

A special task was designed for the use of the Duet™ System with the UroVysion™ Kit, defining filters, classes and stop criteria in accordance with the UroVysion™ Kit. In addition, specific instructions for scanning and analysis of the UroVysion™ Kit were added to the Duet™ User's manual. The performance studies described below confirms that any minor differences between the manual and the automated Duet™ System do not raise any issue of safety or efficacy.

Performance characteristics of the Duet System:

Performance characteristics of the Duet System were verified by the following studies:

- **Study 1 – Comparison of the Duet™ System method to manual scoring method**

This study was performed to demonstrate the equivalency of the Duet™ method to the manual scoring method for detection and enumeration of slides probed by the Vysis Urovysion™ Bladder Cancer Recurrence Kit.

Total of 135 slides were probed using the Vysis UroVysion™ Bladder Cancer Recurrence Kit according to the manufacturer instructions (Vysis Inc., Downers Grove, IL). The slides were screened both manually and using the Duet™ system, while the slides at one of the laboratories were screened

twice for each method. Statistical analysis was performed for each study separately and for the pooled results (178 slides).

The statistical analysis performed included acceptable accuracy analysis with calculation of positive/negative predictive values, combined with Kappa value for agreement level.

High correlation was found between the results of the manual method and the Duet™ Method, showing excellent accuracy in detecting both normal and abnormal samples, as defined by the manual method. The overall agreement level between both methods (described by Kappa agreement level index) was calculated to be 0.918 (P-value<0.0001), with 96.2% agreement in observing "FISH Positive" and 95.7% in observing "FISH negative". No significant differences were found between results from different sites.

The comparison between the Duet™ method and the manual microscopy method demonstrated that the Duet™ system is effective and suitable for distinguishing between FISH negative and FISH positive urine specimens from subjects with transitional cell carcinoma of the bladder, probed by the Vysis UroVysion Bladder Cancer recurrence Kit.

- **Study 2 - Evaluation the performance of the Duet™ System in terms of reproducibility and repeatability, within a system and across systems.**

The reproducibility and repeatability analysis was performed to evaluate the precision of the Duet™ System in the detection and enumeration of transitional cell carcinoma of the bladder, probed by the Vysis UroVysion Bladder Cancer recurrence Kit.

The experiment included four (4) slides, such that each slide was analyzed on three (3) different systems and three (3) times on one of these systems. The slides were selected to cover the range of the intended use, namely, to include two (2) negative slides, one (1) positive and one (1) near the medical decision cutoff. The experiment was performed by two (2) operators at BioView Lab, in cooperation with Meir Hospital, Kfar Saba, Israel.

System reliability, measured by its consistency, in terms of reproducibility and repeatability, was demonstrated by calculating the percentage of agreement between measurements. A high, value indicates a small variance between different runs on the same machine, relative to the differences between machines. The calculated results of the variance within the measurements using the same Duet™ system revealed 100% agreement (12 out of 12), while 91.7% (11 out of 12) agreement between systems was revealed. The overall agreement level was found to be 95.0%. Therefore it

can be concluded that the Duet™ System had proven to have high values of both repeatability and reproducibility.

Conclusion:

Bioview Ltd. believes that the Duet™ System is substantially equivalent to the combination of its predicate devices in terms of Intended Use, Indications for Use, technological characteristics and mode of operation. Any minor differences between the Duet™ System and its predicate devices do not raise new safety or effectiveness issues, based on the performance results and the analysis of similarities and differences presented above.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

AUG 16 2005

Bioview Ltd.
c/o Dorit Winitz, Ph.D.
Biomedical Strategy Ltd.
11 Menachem Begin Street
Ramat Gan, 52521 Israel

Re: k050840
Trade/Device Name: Duet™ system
Regulation Number: 21 CFR 864.5260
Regulation Name: Automated cell-locating device
Regulatory Class: Class II
Product Code: JOY
Dated: March 28, 2005
Received: April 13, 2005

Dear Dr. Winitz:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).
This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html

Sincerely yours,

Robert L. Becker, Jr., MD, Ph.D
Director
Division of Immunology and Hematology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

INDICATIONS FOR USE

510(k) Number (if known): K050840

Device Name: Duet™ system

Indications for Use: The Duet™ System is an automated scanning microscope and image analysis system. It is intended for *in-vitro* diagnostic use as an aiding tool to the pathologist in the detection, classification and counting of cells of interest based on color, intensity, size, pattern, and shape. The Duet™ System is intended to detect:

1. Hematopoietic cells stained by Giemsa stain, Immunohistochemistry or ISH (with bright field and fluorescent) prepared from cell suspension.

2. Amniotic cells stained by FISH (using direct labeled DNA probes for chromosomes X, Y, 13, 18 and 21).

3. Cells in urine specimens, stained by FISH (using the Vysis UroVysion™ Bladder Cancer Recurrence Kit for chromosomes 3, 7, 17 and 9p21 locus), from subjects with transitional cell carcinoma of the bladder.

Prescription Use __√__ AND/OR Over-The-Counter Use____
(Part 21 C.F.R. 801 Subpart D) (Part 21 C.F.R. 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K050840 7-10